IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	)	
	)	
Manfred BOHN et al.	)	Group Art Unit: 1618
	)	
Application No.: 10/606,229	)	Examiner: L. Schlientz
	)	
Filed: June 26, 2003	)	Confirmation No.: 4228
	)	
For: USE OF 1-HYDROXY-2-PYRIDONES FOR THE TREATMENT OF SEBORRHEIC DERMATITIS	)	

Mail Stop Appeal Brief—Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPEAL BRIEF UNDER 37 C.F.R. § 41.37

Pursuant to the Notice of Appeal filed on June 14, 2007, Appellants submit this Appeal Brief in accordance with 37 C.F.R. § 41.37, and enclose herewith the fee of $510.00 required under 37 C.F.R. § 41.20(b)(2). Appellants also file herewith a petition for a two month extension of time herewith, extending the period for filing the Appeal Brief to October 14, 2007, a Sunday.

Table of Contents

I. Real Party in Interest

Sanofi-Aventis Deutschland GmbH is the assignee of record, as evidenced by the assignment recorded July 19, 2006, at Reel 017946, Frame 0877, and has licensed the invention under appeal to Medicis Pharmaceutical Corporation. As such, Sanofi-Aventis Deutschland GmbH and Medicis Pharmaceutical Corporation are real parties in interest in this appeal.

II. Related Appeals and Interferences

With respect to appeals, interferences, or proceedings that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal, Appellants and Appellants' undersigned legal representative inform the Board of the Board's prior Decision in Appeal No. 2004-0309 (in parent application no. 09/077,194), mailed September 15, 2004, copy attached in the Related Proceedings Appendix at the end of this Brief. Also, Appellants filed a Notice of Appeal in application no. 09/077,194 on July 24, 2007, and intend to file an Appeal Brief in due time.

III. Status of Claims

Claims 14-23 and 26-29 are pending and listed in the Claims Appendix of Part VIII. Claims 1-13, 24, and 25 are cancelled.

The Examiner has rejected claims 14-23 and 26-29 under 35 U.S.C. § 103(a).

Claims 14-23 and 26-29 are the subject of this appeal. As argued below, Appellants believe that the rejected claims are patentable.

IV. Status of Amendments

All amendments have been entered. No amendments have been made subsequent to the Reply After Final Under 37 C.F.R. § 1.113 filed April 16, 2007.

V. Summary of Claimed Subject Matter

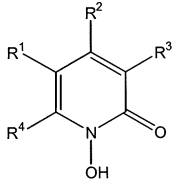
Seborrheic dermatitis ("SD") is a disorder of the scalp, which differs from dandruff by the presence of erythema (i.e., redness) as a sign of inflammation, by a greater degree of scaling with itching and burning, and by eczematous changes at other body sites besides the scalp. *See* specification at p. 1, ll. 3-7. On the scalp, SD can manifest in the form of patches, or affect the whole scalp and beyond, and can be accompanied by secondary infections. *Id.* at ll. 7-11. In contrast, dandruff is characterized by a clinically *noninflammatory* scaling of the scalp and occurs in almost all people. *Id.* at ll. 22-24 (emphasis added).

It is known that 1-hydroxy-2-pyridones exhibit activity against normal dandruff. *Id.* SD, however, was treated by other types of compounds, namely corticosteroids and antimycotics. *Id.* at ll. 26-28. The methods of the present invention use at least one 1-hydroxy-2-pyridone in the treatment of SD. The 1-hydroxy-2-pyridones described in the methods according to the invention as recited in the claims on appeal have several advantages over other treatments for SD. First, 1-hydroxy-2-pyridones exhibit both noninflammatory activity and antimycotic activity. *Id.* at ll. 30-37. Second, 1-hydroxy-2-pyridones have relatively broad anti-bacterial activity in that they are effective against Gram-positive and Gram-negative aerobic and anaerobic bacteria, which can be important when, as often happens, secondary infections are involved in SD cases. *Id.* at p. 2, ll. 6-12. Finally, the solubility of 1-hydroxy-2-pyridones in water, alcohols, and

aqueous-alcoholic solutions makes preparation of lotions and gels simpler. *Id.* at ll. 14-19.

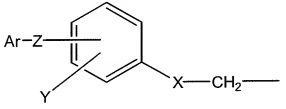
Independent claim 14 is directed to a method of treating seborrheic dermatitis comprising administering to a human seborrheic dermatitis patient an amount effective for the treatment of seborrheic dermatitis of a composition comprising:

(A) a sole active component consisting of at least one 1-hydroxy-2-pyridone of formula I, wherein the at least one 1-hydroxy-2-pyridone is present in free form or as a pharmaceutically acceptable salt:



(I)

where R^1, R^2, and R^3, which are identical or different, are H or alkyl having 1 to 4 carbon atoms, and R^4 is a saturated hydrocarbon radical having 6 to 9 carbon atoms or a radical of formula II:



(II)

where:

X is S or O;

Y is H, or 1 or 2 identical halogen atoms, or a mixture of 2 different halogen atoms;

Z is a single bond, or a linking radical comprising

(1) O, or

(2) S, or

(3) $-CR_2-$, where R is H or (C_1-C_4)-alkyl, or

(4) from 2 to 10 carbon atoms linked in the form of a straight or branched chain, which optionally further comprises one or more of the following:

(i) carbon-carbon double bond, and

(ii) O, S, or a mixture thereof, wherein if 2 or more O or S atoms or a mixture thereof are present, each O or S atom is separated by at least 2 carbon atoms; and,

in any of the foregoing linking radicals, any remaining free valences of the carbon atoms of said linking radical are saturated by H, (C_1-C_4)-alkyl, or a mixture thereof; and

Ar is an aromatic ring system having one or two rings, the aromatic ring system being unsubstituted or substituted by one, two, or three radicals, which are identical or different, and are chosen from halogen, methoxy, (C_1-C_4)-alkyl, trifluoromethyl, and trifluoromethoxy; and

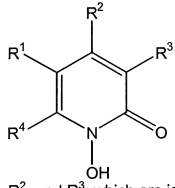
(B) at least one surfactant chosen from anionic surfactants, cationic surfactants, nonionic surfactants, and amphoteric surfactants;

wherein the composition has a pH ranging from about 4.5 to about 6.5; and

wherein the composition is a single composition. *See, e.g.,* specification at p. 2, l. 25 to p. 3, l. 18; p. 5, l. 37 to p. 7, l. 34; p. 8, ll. 29-33; p. 9, l. 17, and Example 8.

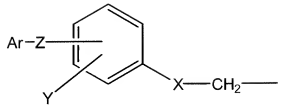
Independent claim 19 is directed to a method of treating seborrheic dermatitis comprising administering to a human seborrheic dermatitis patient an amount effective for the treatment of seborrheic dermatitis of a composition comprising:

(A) a sole active component consisting of at least one 1-hydroxy-2-pyridone of formula I, wherein the at least one 1-hydroxy-2-pyridone is present in free form or as a pharmaceutically acceptable salt:



(I)

where R^1, R^2, and R^3, which are identical or different, are H or alkyl having 1 to 4 carbon atoms, and R^4 is a saturated hydrocarbon radical having 6 to 9 carbon atoms or a radical of formula II:



(II)

where:

X is S or O;

Y is H, or 1 or 2 identical halogen atoms, or a mixture of 2 different halogen atoms;

Z is a single bond, or a linking radical comprising

(1) O, or

(2) S, or

(3) $-CR_2-$, where R is H or (C_1-C_4)-alkyl, or

(4) from 2 to 10 carbon atoms liked in the form of a straight or branched chain, which optionally further comprises one or more of the following:

(i) a carbon-carbon double bond, and

(ii) O, S, or a mixture thereof, wherein if 2 or more O or S atoms or a mixture thereof are present, each O or S atom is separated by at least 2 carbon atoms; and,

in any of the foregoing linking radicals, any remaining free valences of the carbon atoms of said linking radical are saturated by H, (C_1-C_4)-alkyl, or a mixture thereof;

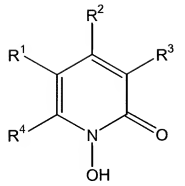
and

Ar is an aromatic ring system having one or two rings, the aromatic ring system being unsubstituted or substituted by one, two, or three radicals, which are identical or different, and are chosen from halogen, methoxy, (C_1-C_4)-alkyl, trifluoromethyl, and trifluoromethoxy; and

(B) at least one surfactant chosen from anionic surfactants, cationic surfactants, nonionic surfactants, and amphoteric surfactants;

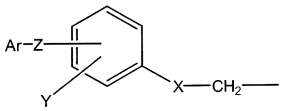
wherein the composition has a pH ranging from about 4.5 to about 6.5; and wherein the composition is a single composition, which is a shampoo. *See, e.g., id.* p. 2, l. 25 to p. 3, l. 18; p. 5, l. 26; p. 5, l. 37 to p. 7, l. 34; p. 8, ll. 29-33; p. 9, l. 17, and Example 8.

Independent claim 26 is directed to a method of treating seborrheic dermatitis comprising administering to a human seborrheic dermatitis patient an amount effective for the treatment of seborrheic dermatitis of a composition comprising:
a sole active component consisting of at least one 1-hydroxy-2-pyridone of formula I, wherein the at least one 1-hydroxy-2-pyridone is present in free form or as a pharmaceutically acceptable salt:



(I)

wherein R^1, R^2 and R^3, which are identical or different, are H or alkyl having 1 to 4 carbon atoms, and R^4 is a saturated hydrocarbon radical having 6 to 9 carbon atoms or a radical of formula II:



(II)

where:

X is S or O;

Y is H, or 1 or 2 identical halogen atoms, or a mixture of 2 different halogen atoms;

Z is a single bond, or

a linking radical comprising

(1) O, or

(2) S, or

(3) $–CR_2$-, where R is H or (C_1-C_4)-alkyl, or

(4) from 2 to 10 carbon atoms linked in the form of a straight or branched chain, which optionally further comprises one or more of the following:

(i) carbon-carbon double bond, and

(ii) O, S, or a mixture thereof, wherein if 2 or more O or S atoms or a mixture thereof are present, each O or S atom is separated by at least 2 carbon atoms; and

in any of the foregoing linking radicals, any remaining free valences of the carbon atoms of said linking radical are saturated by H, (C_1-C_4)-alkyl, or a mixture thereof; and

Ar is an aromatic ring system having one or two rings, the aromatic ring system being unsubstituted or substituted by one, two or three radicals, which are identical or different, and are chosen from halogen, methoxy, (C_1-C_4)-alkyl, trifluoromethyl, and trifluoromethoxy; and

wherein the composition comprises a foam. *See, e.g., id.* at p. 2, l. 25 to p. 3, l. 18; p. 8, l. 15; and Example 8.

VI. Grounds of Rejection to be Reviewed

Claims 14-23 and 26-29 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 4,185,106 ("*Dittmar*") in view of Hanel et al. (*Mycoses* 34 (Supp) 1:91-93 (1991), abstract only) ("*Hanel*") and a "medical dictionary" or U.S. Patent No. 5,834,409 ("*Ramachanddran*"). Final Office Action dated December 15, 2006, at 3.

VII. Argument

A. Claims 14-23 and 26-29 Are Patentable Under 35 U.S.C. § 103(a) Over *Dittmar* in view of *Hanel* and a Medical Dictionary or *Ramachanddran*

Claims 14-23 and 26-29 have been rejected under 35 U.S.C. § 103(a) as obvious over *Dittmar* in view of *Hanel* and a medical dictionary or *Ramachanddran*. The claims on appeal are directed to a method of treating *seborrheic dermatitis* (SD) comprising administering to a human *seborrheic dermatitis* patient an effective amount of the 1-hydroxy-2-pyridone compounds recited in the claims. In contrast, the primary reference relied upon by the Examiner, *Dittmar*, relates to treating *dandruff* with 1-hydroxy-2-pyridones. SD and dandruff are two entirely different conditions, a point Appellants have emphasized repeatedly during prosecution. *See* Amendment filed September 7, 2006, at 14 and 15; Reply filed April 16, 2007, at 4, first paragraph. A reference using 1-hydroxy-2-pyridones to treat dandruff does not make obvious a method of treating a different disorder, i.e., SD.

During prosecution, the Examiner repeatedly acknowledged that *Dittmar* does not teach a method for treating SD, and relies on *Hanel*, which discusses the treatment of seborrheic eczema, to remedy the shortcomings of *Dittmar*. The Examiner then attempted to link seborrheic eczema to seborrheic dermatitis by referencing an on-line medical dictionary. Appellants maintain that even if one of ordinary skill in the art did consider seborrheic eczema to be the same condition as SD, there is still no nexus between *Dittmar*'s treatment of dandruff and *Hanel*'s treatment of seborrheic eczema. Appellants provide further detail and support for their position below. As they will show,

the Examiner has not established a *prima facie* case of obviousness and the rejection of record should be reversed.

1. The Legal Standard

Several basic factual inquiries must be made in order to determine the obviousness or non-obviousness of claims of a patent application under 35 U.S.C. § 103. These factual inquiries, set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), require the Examiner to:

(1) determine the scope and content of the prior art;

(2) ascertain the differences between the prior art and the claims in issue;

(3) resolve the level of ordinary skill in the pertinent art; and

(4) evaluate evidence of secondary considerations.

The obviousness or non-obviousness of the claimed invention is then evaluated in view of the results of these inquiries. *Graham*, 383 U.S. at 17-18, 148 USPQ 467; *see also KSR Int'l Co. v. Teleflex, Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), slip op. at 2.

The Supreme Court, in its recent decision in *KSR Int'l Co. v. Teleflex, Inc.*, recognized that a showing of "teaching, suggestion, or motivation" could provide helpful insight in determining whether the claimed subject matter is obvious under Section 103(a). *KSR,* slip op. at 14. In addition, the Supreme Court mandated that "[t]o facilitate review, this analysis [of whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue] should be made explicit." *Id.* (citing *In re Kahn*, 441 F.3d 977, 988 (Federal Circuit, 2006) ("[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead,

there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness")).

Following the *KSR* decision, the Office issued a memorandum to its technology center directors on May 3, 2007, indicating that **"in formulating a rejection under 35 U.S.C. § 103(a) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed**." (Emphasis in original). Appellants submit that in the present case the Examiner has failed to explain why there would have been motivation for one of ordinary skill in the art to make the proposed combination of prior art elements, and that, regardless of the Examiner's position, no such motivation exists.

2. The Examiner Has Not Established A *Prima Facie* Case of Obviousness

With respect to the scope and content of the prior art, as stated by the Examiner, *Dittmar* teaches an antidandruff treatment using a pharmaceutical composition containing 1-hydroxy-2-pyridones, such as ciclopirox, as an active agent. Final Office Action dated December 15, 2006, at p. 3-4. The Examiner also contends that *Dittmar* teaches a "weakly acidic composition which is desirable for hair composition[s]" and appears to suggest that a weakly acidic pH would be a pH "around 4.5-6.5." *Id.* at 5. The Examiner acknowledges, however, that *Dittmar* differs from the present claims in that he does not teach the use of this composition for treating SD. *Id. at 4.*

Appellants note that *Dittmar* consistently refers to its compositions as "anti-dandruff agents" or "anti-dandruff compositions" that are useful for the "treatment of

dandruff" or for "removing dandruff." See, e.g., col. 1, l. 7; col. 4, ll. 59-63; and col. 6, l. 42. There is no teaching whatsoever in *Dittmar* of a method of treating SD or any suggestion that its compositions could be used in a treatment for SD. Moreover, in admitting that *Dittmar* does not teach the use of the composition for treating SD, the Examiner acknowledges that SD and dandruff are in fact different conditions.

In an effort to fill the gap left by *Dittmar*, the Examiner relies on *Hanel*, contending that this reference teaches that an antimycotic agent such as 1-hydroxy-2-pyridone, for example ciclopirox, was effectively used to treat seborrheic eczema in humans. Final Office Action dated December 15, 2006, at p. 4. According to the Examiner, *Hanel* also teaches "significant therapeutic effectiveness" that is achieved by using ciclopirox where "strong inhibition of inflammation and infiltration and flakiness" was obtained. *Id.* Relying on excerpts from on-line medical dictionaries, the Examiner then asserts that seborrheic eczema is an alternative term for SD. *Id.*; *see also* Advisory Action, where Examiner again refers to these as "similar conditions."

Taking these references in combination, the Examiner concludes that it would have been obvious to one of ordinary skill in the art to extend the alleged teachings of *Dittmar* to include SD. *Id.* The Examiner alleges that the skilled artisan would have been motivated to combine *Dittmar*, *Hanel*, and the cited "medical dictionary" and make the modification because these references are "drawn to the same technical fields [(]

constituted with same ingredients and share common utilities" and are "pertinent to the problem which applicant concerns about."[1] *Id.* at 5

To show a *prima facie* case of obviousness in view of the *Graham* factors set forth above, the Examiner must still meet the requirements of M.P.E.P. §2143. In particular, the Examiner must show, *inter alia,* that there is some suggestion or motivation, either in the references or in the knowledge generally available to one of ordinary skill in the art, to modify or combine cited references. As noted above, in its decision in the *KSR* case, the U.S. Supreme Court stated not only that an explanation of the motivation to combine provides helpful insight in determining obviousness, but also that the Examiner's reasoning and analysis of whether there was an apparent reason to combine the known elements as claimed should be clearly set forth.

In the present case, the Examiner's alleged reasoning is based on generalities of "same technical fields" and "sharing common utilities." These alleged reasons do not speak to the specific teachings of the references invoked by the Examiner. As for the Examiner's suggestion that *Dittmar* and *Hanel* use "the same ingredients," the *Hanel* abstract does not provide a complete description of the composition used in order to allow a useful comparison between the ingredients in *Dittmar*'s composition and the ingredients in *Hanel*'s composition. As Appellant will explain below, there is no motivation to combine *Dittmar*, *Hanel*, and the cited "medical dictionaries" as suggested by the Examiner.

---

[1] Though the *Ramachanddran* patent was mentioned in support of this rejection, the Examiner has not actually applied it against the claims on appeal.

Nothing in the references cited by the Examiner equates dandruff, as discussed in *Dittmar*, and seborrheic eczema, as discussed in *Hanel*. Thus, there is no suggestion or motivation to modify *Dittmar*'s treatment of dandruff for use in treatment of SD. Moreover, even if the Examiner were correct that seborrheic ecezma and SD were equivalent, one of ordinary skill in the art would find no teaching, suggestion or motivation in any of the cited references to modify *Dittmar* for the treatment of SD.

As made clear above, *Dittmar* teaches the treatment of dandruff. Appellants have maintained throughout prosecution the position that dandruff and SD are two different conditions. *See, e.g.,* Amendment filed September 7, 2006, at p. 14 and 15. The declaration of Dr. Mitchell Wortzman, filed on September 7, 2006, clearly distinguishes dandruff from seborrheic dermatitis. Dandruff is a "noninflammatory scaling of the scalp," and seborrheic dermatitis is an "inflammatory, erythematous, and scaling eruption." Wortzman Declaration at page 2. In addition, the scales of dandruff look different from the scales of seborrheic dermatitis. *Id.* The instant specification also clearly teaches that SD and dandruff are distinct and separate conditions. See p. 1, ll. 3-24.

As the Court of Appeals for the Federal Circuit has instructed, when construing the meaning of a term, one should first turn to the intrinsic evidence, that being the specification and the prosecution history. See *Phillips v. AWH Corp.*, 415 F.3d 1303, 1317 (Fed. Cir. 2005) ("However, while extrinsic evidence "can shed useful light on the relevant art," we have explained that it is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'"). Thus, because dandruff and seborrheic eczema are different conditions, as clearly shown by this

evidence of record, the skilled artisan would not have been motivated to modify or combine the teachings of *Dittmar* relating to dandruff with the teachings of *Hanel* relating to seborrheic eczema. As a result, the alleged teachings of the "medical dictionaries" cited by the Examiner that SD and seborrheic ecezma are equivalent are irrelevant to linking the teaching of *Dittmar* to the teaching of *Hanel*.

In sum, because there is no motivation to combine these references as the Examiner suggests, the Examiner has not set forth a *prima facie* case of obviousness.

3. The Examiner Acknowledges the Non-Obviousness of Independent Claims 14, 19, and 26

During prosecution, the Examiner suggested an amendment to claim 14 that she believed would make claim 14 patentable. *See* Reply After Final filed April 16, 2007, at p. 5-6. The Examiner relied on five items to support non-obviousness: (1) a description of Stieprox® Shampoo taken from a consumer medical information website submitted in the IDS filed September 22, 2006, and showing that Stieprox® Shampoo contains anionic (sodium laureth sulphate) and amphoteric (cocamidopropyl betaine) surfactants; (2) a citation from the website www.pharmacychecker.com, which incorrectly states that Loprox® Shampoo and Stieprox® Shampoo (in Canada) have the same formula; (3) Example 2 of the instant specification, showing a shampoo containing ciclopirox, an anionic surfactant, and an amphoteric surfactant; (4) a teaching in the specification at page 6 of the "importance" of amphoteric surfactants "for the optimization of" anionic surfactants; and (5) Applicant's statements on the commercial success of Loprox® Shampoo, particularly at page 13 of the Supplemental Response filed September 22, 2006, and the Declaration of Mr. Kevin Kriel.

The Examiner acknowledged the unexpected commercial success of the use of Loprox® Shampoo. *See id.*, Exhibit A. The Examiner, however, incorrectly assumed that Stieprox® Shampoo was Appellant's commercial embodiment. As Appellants explained, Stieprox® Shampoo contains different surfactants than are used in Loprox® Shampoo. *See id.*, at p. 7. But the Examiner's rationale can be used to support the patentability of both Stieprox® Shampoo and Loprox® Shampoo. The use of both products to treat SD falls within the scope of the pending claims. Both Loprox® Shampoo and Stieprox® Shampoo are commercially successful, according to the Examiner and the Kreil declaration. Both products contain the claimed active ingredients, and various different combinations of surfactants, all of which are encompassed in the scope of the claims, showing that the commercial success is actually commensurate with the scope of the claims.

The pending claims cover the use of a specific 1-hydroxy-2-pyridone with any combination of four (4) types of surfactants to treat seborrheic dermatitis. Loprox® Shampoo contains ciclopirox and a combination of nonionic and anionic surfactants. *See id.*, Exhibit B. Stieprox® Shampoo contains ciclopirox and a combination of anionic and amphoteric surfactants. As the Examiner acknowledged, the use of Loprox® Shampoo for treating SD is commercially successful, supporting the non-obviousness of the claimed methods. In the Advisory Action mailed June 26, 2007, however, the Examiner attempted to discount the evidentiary value of the Declaration of Mr. Kevin Kriel, suggesting that Mr. Kriel's statements on the commercial success of Loprox® Shampoo were not commensurate in scope with the claims on appeal. *See* p. 2. Appellants note that the Examiner cited MPEP §716.03. *See id.* MPEP §716.03(a)

instructs that "[i]n order to be commensurate in scope with the claims, the commercial success must be due to claimed features, and not due to unclaimed features." Mr. Kriel's Declaration discusses the commercial success of Loprox® Shampoo, which falls within the scope of the features of the claims on appeal. Moreover, Mr. Kriel's Declaration should be considered in light of all the evidence of record. For example, the use of Stieprox® Shampoo on SD is also commercially successful outside the U.S. (as reflected in the website cited by the Examiner). Because the Examiner's rationale can be used to support the patentability of both Stieprox® Shampoo and Loprox® Shampoo and the use of both products to treat SD falls within the scope of the pending claims, Appellants submit that, for this additional reason, the claims on appeal are not obvious in light of *Dittmar*, *Hanel*, and the "medical dictionaries" cited by the Examiner.

B. Conclusion

In view of the arguments above and on the record, Appellants respectfully request that the outstanding rejection in this case be reversed.

To the extent any extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this Appeal Brief, such extension is hereby respectfully requested. If there are any fees due under 37 C.F.R. §§ 1.16 or 1.17 which are not enclosed herewith, including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge such fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: October 15, 2007

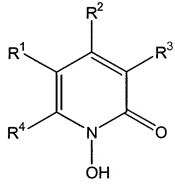
By: Thalia V. Warnement
Reg. No. 39,064

VIII. Claims Appendix

1-13. (Canceled).

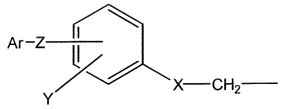
14. A method of treating seborrheic dermatitis comprising administering to a human seborrheic dermatitis patient an amount effective for the treatment of seborrheic dermatitis of a composition comprising:

(A) a sole active component consisting of at least one 1-hydroxy-2-pyridone of formula I, wherein the at least one 1-hydroxy-2-pyridone is present in free form or as a pharmaceutically acceptable salt:



(I)

where R^1, R^2, and R^3, which are identical or different, are H or alkyl having 1 to 4 carbon atoms, and R^4 is a saturated hydrocarbon radical having 6 to 9 carbon atoms or a radical of formula II:



(II)

where:

X is S or O;

Y is H, or 1 or 2 identical halogen atoms, or a mixture of 2 different halogen atoms;

Z is a single bond, or a linking radical comprising

(1) O, or

(2) S, or

(3) $-CR_2-$, where R is H or (C_1-C_4)-alkyl, or

(4) from 2 to 10 carbon atoms linked in the form of a straight or branched chain, which optionally further comprises one or more of the following:

(i) carbon-carbon double bond, and

(ii) O, S, or a mixture thereof, wherein if 2 or more O or S atoms or a mixture thereof are present, each O or S atom is separated by at least 2 carbon atoms; and,

in any of the foregoing linking radicals, any remaining free valences of the carbon atoms of said linking radical are saturated by H, (C_1-C_4)-alkyl, or a mixture thereof; and

Ar is an aromatic ring system having one or two rings, the aromatic ring system being unsubstituted or substituted by one, two, or three radicals, which are identical or different, and are chosen from halogen, methoxy, (C_1-C_4)-alkyl, trifluoromethyl, and trifluoromethoxy; and

(B) at least one surfactant chosen from anionic surfactants, cationic surfactants, nonionic surfactants, and amphoteric surfactants;

wherein the composition has a pH ranging from about 4.5 to about 6.5; and

wherein the composition is a single composition.

15. A method of treating seborrheic dermatitis as claimed in claim 14 in which the at least one 1-hydroxy-2-pyridone of formula I comprises a cyclohexyl radical in the R^4 position.

16. A method of treating seborrheic dermatitis as claimed in claim 14 in which the at least one 1-hydroxy-2-pyridone of formula I comprises an octyl radical of the formula $-CH_2-CH(CH_3)-CH_2-C(CH_3)_3$ in the R^4 position.

17. A method of treating seborrheic dermatitis as claimed in claim 14 in which the composition comprises

1-hydroxy-4-methyl-6-(4-(4-chlorophenoxy)phenoxymethyl)-2(1H)pyridone,

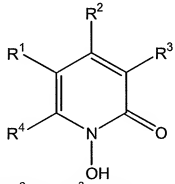
1-hydroxy-4-methyl-6-cyclohexyl-2(1H)pyridone, or

1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2(1H)pyridone, or a pharmaceutically acceptable salt of any of the foregoing, or a mixture of any of the foregoing.

18. A method of treating seborrheic dermatitis as claimed in claim 14 in which the composition further comprises at least one additional surfactant chosen from anionic, cationic, nonionic, and amphoteric surfactants.

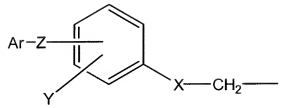
19. A method of treating seborrheic dermatitis comprising administering to a human seborrheic dermatitis patient an amount effective for the treatment of seborrheic dermatitis of a composition comprising:

(A) a sole active component consisting of at least one 1-hydroxy-2-pyridone of formula I, wherein the at least one 1-hydroxy-2-pyridone is present in free form or as a pharmaceutically acceptable salt:



(I)

where R^1, R^2, and R^3, which are identical or different, are H or alkyl having 1 to 4 carbon atoms, and R^4 is a saturated hydrocarbon radical having 6 to 9 carbon atoms or a radical of formula II:



(II)

where:

X is S or O;

Y is H, or 1 or 2 identical halogen atoms, or a mixture of 2 different halogen atoms;

Z is a single bond, or a linking radical comprising

(1) O, or

(2) S, or

(3) $-CR_2-$, where R is H or (C_1-C_4)-alkyl, or

(4) from 2 to 10 carbon atoms liked in the form of a straight or branched chain, which optionally further comprises one or more of the following:

(i) a carbon-carbon double bond, and

(ii) O, S, or a mixture thereof, wherein if 2 or more O or S atoms or a mixture thereof are present, each O or S atom is separated by at least 2 carbon atoms; and,

in any of the foregoing linking radicals, any remaining free valences of the carbon atoms of said linking radical are saturated by H, (C_1-C_4)-alkyl, or a mixture thereof;

and

Ar is an aromatic ring system having one or two rings, the aromatic ring system being unsubstituted or substituted by one, two, or three radicals, which are identical or different, and are chosen from halogen, methoxy, (C_1-C_4)-alkyl, trifluoromethyl, and trifluoromethoxy; and

(B) at least one surfactant chosen from anionic surfactants, cationic surfactants, nonionic surfactants, and amphoteric surfactants;

wherein the composition has a pH ranging from about 4.5 to about 6.5; and

wherein the composition is a single composition, which is a shampoo.

20. A method of treating seborrheic dermatitis as claimed in claim 19 in which the at least one 1-hydroxy-2-pyridone of formula I comprises a cyclohexyl radical in the R^4 position.

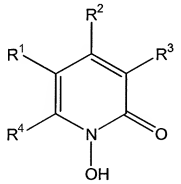
21. A method of treating seborrheic dermatitis as claimed in claim 19 in which the at least one 1-hydroxy-2-pyridone of formula I comprises an octyl radical of the formula -CH_2-$CH(CH_3)$-CH_2-$C(CH_3)_3$ in the R^4 position.

22. A method of treating seborrheic dermatitis as claimed in claim 19 in which the composition comprises 1-hydroxy-4-methyl-6-(4-(4-chlorophenoxy)phenoxymethyl)-2(1H)pyridone, 1-hydroxy-4-methyl-6-cyclohexyl-2(1H)pyridone, or 1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2(1H)pyridone, or a pharmaceutically acceptable salt of any of the foregoing, or a mixture of any of the foregoing.

23. A method of treating seborrheic dermatitis as claimed in claim 19 in which the composition further comprises at least one additional surfactant chosen from anionic, cationic, nonionic, and amphoteric surfactants.

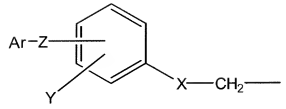
24 and 25. (Canceled).

26. A method of treating seborrheic dermatitis comprising administering to a human seborrheic dermatitis patient an amount effective for the treatment of seborrheic dermatitis of a composition comprising:
a sole active component consisting of at least one 1-hydroxy-2-pyridone of formula I, wherein the at least one 1-hydroxy-2-pyridone is present in free form or as a pharmaceutically acceptable salt:



(I)

wherein R^1, R^2 and R^3, which are identical or different, are H or alkyl having 1 to 4 carbon atoms, and R^4 is a saturated hydrocarbon radical having 6 to 9 carbon atoms or a radical of formula II:



(II)

where:

X is S or O;

Y is H, or 1 or 2 identical halogen atoms, or a mixture of 2 different halogen atoms;

Z is a single bond, or

a linking radical comprising

(1) O, or

(2) S, or

(3) $-CR_2-$, where R is H or (C_1-C_4)-alkyl, or

(4) from 2 to 10 carbon atoms linked in the form of a straight or branched chain, which optionally further comprises one or more of the following:

(i) carbon-carbon double bond, and

(ii) O, S, or a mixture thereof, wherein if 2 or more O or S atoms or a mixture thereof are present, each O or S atom is separated by at least 2 carbon atoms; and

in any of the foregoing linking radicals, any remaining free valences of the carbon atoms of said linking radical are saturated by H, (C_1-C_4)-alkyl, or a mixture thereof; and

Ar is an aromatic ring system having one or two rings, the aromatic ring system being unsubstituted or substituted by one, two or three radicals, which are identical or different, and are chosen from halogen, methoxy, (C_1-C_4)-alkyl, trifluoromethyl, and trifluoromethoxy; and

wherein the composition comprises a foam.

27. The method of claim 26 wherein the at least one 1-hydroxy-2-pyridone of formula I comprises a cyclohexyl radical in the R^4 position.

28. The method of claim 26 wherein the at least one 1-hydroxy-2-pyridone of formula I comprises an octyl radical of the formula $-CH_2$-$CH(CH_3)$-CH_2-$C(CH_3)_3$ in the R^4 position.

29. The method of claim 26 wherein the at least one 1-hydroxy-2-pyridone of formula I comprises one compound selected from the group consisting of 1-hydroxy-4-methyl-6-(4-(4-chlorophenoxy)phenoxymethyl)-2-(1H)pyridone, 1-hydroxy-4-methyl-6-cyclohexyl-2(1H)pyridone,1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)2(1H)pyridone, a pharmaceutically acceptable salt of any of the foregoing, and a mixture of any of the foregoing.

IX. Evidence Appendix

1. Declaration of Dr. Mitchell Wortzman, entered by the Examiner with the Amendment filed on September 7, 2006.

2. Declaration of Mr. Kevin Kriel, entered by the Examiner with the Supplemental Response filed on September 22, 2006.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Bohn et al.

Serial No. 09/077,194

Filed: December 4, 1998

Attorney Docket No.: 02-40045-US

USE OF 1-HYDROXY-2-PYRIDONES FOR THE TREATMENT OF SEBORRHEIC DERMATITIS

DECLARATION OF MITCHELL S. WORTZMAN, Ph.D.

I, Mitchell S. Wortzman, hereby declare as follows:

1. I am the Executive Vice President, Research and Development for Medicis Pharmaceutical Corporation ("Medicis"), and have been employed by Medicis since 1997. From 1980 to 1997, I was employed at Neutrogena Corporation, and was the President of the Dermatologics Division starting in 1989.

2. Medicis is a licensee under this patent application.

3. Since 1980 I have been involved in the research and development for numerous dermatological products. My Ph.D. is in cellular and molecular biology from the University of Southern California.

4. I have reviewed the record in this application concerning the differences between dandruff and seborrheic dermatitis. The scientific literature of record correctly

states the understanding in the fields of dermatology and dermatological research that these are separate and distinct conditions. See, the reference cited previously in the above-identified application and attached as Exhibits A.

5. The rest of the scientific literature is in accord with the view that dandruff is a "noninflammatory" scaling of the scalp, while "seborrheic dermatitis is an inflammatory, erythematous, and scaling eruption that occurs in seborrheic areas...such as the scalp, face, and trunk." (See Manual of Dermatologic Therapeutics, Fifth ed., p. 164-167 (1995) attached as Exhibit B).

6. Even the scales of dandruff look different from the scale from seborrheic dermatitis; dandruff has thin, white or gray flakes, while seborrheic dermatitis has oily, yellowish scales with inflammation. (See Handbook of Nonprescription Drugs, p. 550-552 (1996) attached as Exhibit C).

7. One of ordinary skill in the art would not find it obvious to use a certain composition to treat seborrheic dermatitis, merely because the same composition is used to treat dandruff.

8. I am unable to respond to the Examiner's position to the contrary. The Examiner has not addressed the substance of the cited literature, and does not appear to speak on the basis of her own research or clinical experience. Without any basis for her rejection of the well-settled understanding of those in the art, I cannot know why she has taken this mistaken position, how to explain the source of her error, or what evidence would convince her that her position is incorrect. The most that one can say is that the Examiner appears to have taken a position on the

basis of her own belief that is contrary to the scientific literature of record and my own long experience in the field.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application and any registration resulting therefrom.

Mitchell S. Wortzman, Ph.D.

Date: 6/6/03

Appendix A

CHAPTER 126 - Seborrheic Dermatitis

Gerd Plewig
Thomas Jansen

Seborrheic dermatitis is a common, chronic papulosquamous dermatosis that is usually easily recognized. It affects infants and adults and is often associated with increased sebum production (seborrhea) of the scalp and the sebaceous follicle–rich areas of the face and trunk. The affected skin is pink, edematous, and covered with yellow-brown scales and crusts. The disease has a wide range from mild to severe, including psoriasiform or pityriasiform patterns and erythroderma.[1,2,3,4,5] Seborrheic dermatitis is one of the most common skin manifestations in patients with HIV infection.[6,7,8,9] It is therefore included in the spectrum of premonitory lesions and should be carefully evaluated in high-risk patients.

Incidence

Seborrheic dermatitis has two age peaks, one in infancy within the first 3 months of life and the second around the fourth to the seventh decade of life. No data are available on the exact incidence of seborrheic dermatitis in infants, but the disorder is common. The disease in adults is believed to be more common than psoriasis, for example, affecting at least 2 to 5 percent of the population. Men are affected more often than women in all age groups. There does not appear to be any racial predilection. Seborrheic dermatitis is one of the most common diseases associated with HIV infection as it is found in up to 85 percent of these patients.[7]

Etiology and Pathogenesis

Although many theories abound, the cause of seborrheic dermatitis remains unknown.

Seborrhea

The disease is associated with oily-looking skin (seborrhea oleosa), although increased sebum production cannot always be detected in these patients.[10] Even if seborrhea does provide a predisposition, seborrheic dermatitis is not a disease of the sebaceous glands. The high incidence of seborrheic dermatitis in newborns parallels the size and activity of the sebaceous glands at this age. It has been shown that newborns have large

sebaceous glands with high sebum secretion rates.[11] In childhood, sebum production and seborrheic dermatitis are closely connected. In adulthood, however, they are not, as the sebaceous gland activity peaks in early puberty and seborrheic dermatitis may not occur until decades later.

The sites of predilection—face, ears, scalp, and upper part of the trunk—are particularly rich in sebaceous follicles. Two diseases are prevalent in these regions: seborrheic dermatitis and acne. In patients with seborrheic dermatitis, the sebaceous glands are often particularly large on cross-sectional histologic specimens. In one study, skin surface lipids were not elevated but the lipid composition was characterized by an increased proportion of cholesterol, triglycerides, and paraffin and a decrease in squalene, free fatty acids, and wax esters.[12] Seborrheic dermatitis seems to be more frequent in patients with parkinsonism, in whom sebum secretion is increased, and after treatment with levodopa and a reduction of skin oiliness, seborrheic dermatitis may be improved.[13]

The synonym *eczéma flannellaire* stems from the idea that a retention of skin surface lipids by clothing—cotton (flannel), wool, or synthetic underwear in particular—promotes or aggravates seborrheic dermatitis.

Microbial Effects

Unna and Sabouraud, who were among the first to describe the disease, favored an etiology involving bacteria, yeasts, or both. This hypothesis has remained unsupported, although bacteria and yeasts can be isolated in great quantities from affected skin sites.

In infancy, *Candida albicans* is often found in dermatitic skin lesions and in stool specimens. Intracutaneous tests with candidin, positive agglutinating antibodies in serum, and positive lymphocyte-transformation tests in affected infants revealed a sensitization to *C. albicans*. Even so, these observations cannot be convincingly linked to the pathogenesis. Aerobic bacteria were recovered from the scalp of patients with seborrheic dermatitis (geometric mean of 140,000/cm^2 versus 280,000 in normal individuals and 250,000 in persons with dandruff). In contrast, *Staphylococcus aureus* was rarely seen in normal persons or those with dandruff. When present, it was recovered in about 20 percent of patients with seborrheic dermatitis, accounting for an average of about 32 percent of the total skin flora.[14]

Propionibacterium acnes counts were low in patients with seborrheic dermatitis (7550 geometric mean/cm^2 in those without dandruff). The

small quantities of *P. acnes* in patients with seborrheic dermatitis may explain the low yield of free fatty acids from their skin surfaces.

The lipophilic yeast *Pityrosporum* is abundant in normal skin (504,000 geometric mean/cm^2 versus 922,000 in individuals with dandruff and 665,000 in patients with seborrheic dermatitis).[14] This organism has received particular attention in recent years. Some authors claim strong evidence in favor of a pathogenic role for these microbes,[15,16,17] whereas others do not share this view. Their arguments are that *P. ovale* is not the causative organism but is merely present in large numbers. Clearing of seborrheic dermatitis by selenium sulfide and continued suppression of *P. ovale* with topical amphotericin B caused a relapse of the disease on inflamed scalp skin.[17] In seborrheic dermatitis, both normal[18] and high[19] levels of serum antibodies against *P. ovale* have been demonstrated. A cell-mediated immune response to *P. ovale* has been found in normal individuals using *Pityrosporum* extracts in lymphocyte-transformation studies.[20] Others have demonstrated an association between strong skin colonization with *P. ovale* and altered cellular immunity.[21] Overgrowth of *P. ovale* may lead to inflammation, either through introduction of yeast-derived metabolic products into the epidermis or as a result of the presence of yeast cells on the skin surface. The mechanism of production of inflammation would likely then be through Langerhans cell and T lymphocyte activation by *Pityrosporum* or its byproducts. When *P. ovale* comes into contact with serum, it can activate complement via the direct and alternative pathways, and this may play some part in the introduction of inflammation.[22]

Miscellaneous

Drugs

Several drugs have been reported to produce seborrheic dermatitis–like lesions, including arsenic, gold, methyldopa, cimetidine, and neuroleptics.[23,24]

Neurotransmitter abnormalities

Seborrheic dermatitis is often associated with a variety of neurologic abnormalities, pointing to a possible influence of the nervous system.[25,26] These neurologic conditions include postencephalitic parkinsonism, epilepsy, supraorbital injury, facial paralysis, unilateral injury to the ganglion of Gasser, poliomyelitis, syringomyelia, and quadriplegia. Emotional stress seems to aggravate the disease; a high rate of seborrhea is reported among combat troops in times of war.

Physical factors

Seasonal variations in temperature and humidity are related to the course of the disease. Low autumn and winter temperatures and low humidity in centrally heated rooms are known to worsen the condition. Seborrheic dermatitis of the face was observed in 8 percent of 347 patients receiving PUVA therapy for psoriasis and occurred within a few days to 2 weeks after the beginning of treatment[22]; the patients had no previous history of facial psoriasis or seborrheic dermatitis. Lesions were avoided by masking the face during irradiation.

Aberrant epidermal proliferation

Epidermal proliferation is increased in seborrheic dermatitis, like psoriasis, which explains why cytostatic therapeutic modalities may improve the condition.[23]

Nutritional Disorders

Zinc deficiency in patients with acrodermatitis enteropathica and acrodermatitis enteropathica-like conditions may be accompanied by dermatitis mimicking seborrheic dermatitis of the face. Seborrheic dermatitis, however, is not associated with zinc deficiency nor does it respond to supplementary zinc therapy. Seborrheic dermatitis in infancy may have a different pathogenesis. Biotin deficiency, whether secondary to a holocarboxylase deficiency or a biotinidase deficiency, and abnormal metabolism of essential fatty acids[23] have been proposed as possible mechanisms.

Immunodeficiency and Seborrheic Dermatitis

The development of seborrheic dermatitis either de novo or as a flare of preexisting disease may also serve as a clue to the presence of HIV infection. The first report of this association in 1984[6] was followed by observations from all parts of the world.[7,8] The expression of the disease differs in several aspects from the classic form seen in HIV-seronegative individuals (Figs. 126-1, 126-2, 126-3, and 126-4). The distribution is extensive, severity remarkable, and treatment often difficult (Fig. 126-5). Even the histologic changes differ somewhat from those seen in commonly encountered seborrheic dermatitis (Table 126-1).[2]

The increased incidence and severity of seborrheic dermatitis in HIV-seropositive individuals has led to speculation that unchecked growth of *Pityrosporum* in immunosuppressed patients is responsible. However,

studies that compared quantitative *Pityrosporum* cultures in AIDS patients with and without seborrheic dermatitis either failed to demonstrate increased yeast colonization in patients with seborrheic dermatitis[30] or yielded only a weak correlation between yeast colonization and seborrheic dermatitis.[31]

Psoriasis and Seborrheic Dermatitis

In patients with a psoriatic diathesis, particularly adults, seborrheic dermatitis is said to evolve into psoriasis. The term *sebopsoriasis* is sometimes used for these overlapping conditions. It should be used with caution because psoriasis, especially of the scalp, is clinically and histologically almost indistinguishable from seborrheic dermatitis.

Pityriasis Amiantacea

Pityriasis amiantacea (also known as tinea amiantacea, porrigo amiantacea, tinea asbestina, fausse teigne amiantacée, keratosis follicularis amiantacea) is the name given to a disease of the scalp in which heavy scales extend onto the hairs and separate and bind together their proximal portions (Fig. 126-6).

Pityriasis amiantacea is a reaction of the scalp, often without evident cause, that may occur at any age. It may be observed as a complication or sequel of streptococcal infection, seborrheic dermatitis, atopic dermatitis, or lichen simplex and it also occurs in psoriasis, of which it may be the first clinical manifestation.[32,33] The process may be circumscribed or diffuse. It is only slightly inflammatory, with dry, micaceous scales, or markedly inflammatory, with admixture of a crust. Removal of the scales reveals normal or erythematous, edematous epidermis. The process is not followed by atrophy, scarring, or alopecia. If scarring alopecia occurs, it may be related to secondary infection.

A common form complicates chronic or recurrent fissuring behind one or both ears, mostly in young girls, with the sticky scales extending several centimeters into the neighboring scalp. Another form extends upward from patches of lichen simplex and is seen mainly in middle-aged women.

Histopathology

The histologic picture varies according to the stage of the disease, i.e., acute, subacute, or chronic.[34,35,36] In acute and subacute seborrheic dermatitis, there is a sparse superficial perivascular infiltrate of lymphocytes and histiocytes, slight to moderate spongiosis, slight psoriasiform

hyperplasia, follicular plugging by orthokeratosis and parakeratosis, and scale-crusts containing neutrophils at the tips of the follicular ostia (see Table 126-1). In chronic seborrheic dermatitis, there are markedly dilated capillaries and venules in the superficial plexus in addition to the above-mentioned features.

Clinically and histologically, the lesions of chronic seborrheic dermatitis are psoriasiform and often difficult to distinguish from those of psoriasis.[24] Abortive forms of psoriasis share many features with seborrheic dermatitis. There are lesions that resemble psoriasis and may persist over many years before they finally turn into overt psoriasis. The most important diagnostic signs of seborrheic dermatitis are mounds of scale-crust containing neutrophils at the tips of the dilated horn-filled follicular infundibula. Acrosyringia and acroinfundibula may be plugged by corneocyte casts.

The most consistent findings in pityriasis amiantacea are spongiosis, parakeratosis, migration of lymphocytes into the epidermis, and a variable degree of acanthosis.[23] The essential feature responsible for the asbestos-like scaling are diffuse hyperkeratosis and parakeratosis together with follicular keratosis surrounding each hair by a sheath of corneocytes and debris.

Exfoliative Cytology

Cytologic abnormalities of superficial horny cells (corneocytes), including ortho- and parakeratotic (nucleated) cells, horny cells in different stages of nuclear decomposition (halo cells), and masses of leukocytes, can be evaluated by exfoliative cytology. Seborrheic dermatitis and psoriasis, however, present similar findings compared with other conditions of the dermatitis-eczema group.[27]

Clinical Findings

In all patients with seborrheic dermatitis there is a so-called seborrheic stage, often combined with a gray-white or yellow-red skin discoloration, prominent follicular openings, and mild to severe pityriasiform scales. Several forms can be distinguished (Table 126-2).

Seborrheic Dermatitis in Infants

The disease occurs in infants, predominantly within the first months of life, as an inflammatory disease mainly affecting the hairy scalp and intertriginous folds with greasy-looking scales and crusts. Other regions such as the

center of the face, chest, and neck may also be affected. Scalp involvement is fairly characteristic. The frontal and parietal scalp regions are covered with an oily-looking, thick, often fissured crust [*crusta lactea* (*milk crust*), or *cradle cap*]. Hair loss does not occur, and inflammation is sparse. In the course of the disease, the redness increases and the scaled areas form clearly outlined erythematous patches topped by a greasy scale. Extension beyond the frontal hairline occurs. The retroauricular folds, the pinna of the ear, and the neck may also be involved. Otitis externa is often a complicating factor. Semiocclusive clothing and diapers favor moisture, maceration, and intertriginous dermatitis, particularly in the folds of the neck, axillae, anogenital area, and groin. Opportunistic infection with *C. albicans*, *S. aureus*, and other bacteria occurs. The clinical aspect reminds one of psoriasis vulgaris, hence the expressions *psoriasoid psoriasis* or *napkin psoriasis*.[38]

Course

The disease is usually protracted over weeks to months. Exacerbation and, rarely, erythroderma desquamativum may occur. The prognosis is good. There is no indication that infants with seborrheic dermatitis are more likely to suffer from the adult form of the disease.

Differential Diagnosis

The differential diagnosis in seborrheic dermatitis of infancy includes atopic dermatitis (which usually starts after the third month of life); psoriasis in newborns, a rare disease; scabies; and Langerhans cell histiocytosis. The most useful distinguishing feature between atopic dermatitis and seborrheic dermatitis is the increased number of lesions on the forearms and shins in the former and in the axillae in the latter. The development of skin lesions solely in the diaper area favors a diagnosis of infantile seborrheic dermatitis.[22] Radioallergosorbent testing for egg white and milk antibodies or other geographically or ethnically relevant allergens (e.g., soybean) and, to a lesser extent, total IgE levels may be useful in diagnosing atopic dermatitis at an early stage and distinguishing it from infantile seborrheic dermatitis.[48]

Erythroderma Desquamativum (Leiner's Disease)

This complication of seborrheic dermatitis in infants (dermatitis seborrhoides infantum) was described in 1908 by Leiner.[41] There is usually a sudden confluence of lesions leading to a universal scaling redness of the

skin (erythroderma). The young patients are severely ill with anemia, diarrhea, and vomiting. Secondary bacterial infection is common. The disease occurs in both a familial and a nonfamilial form. Patients with the former are noted for having a functional deficiency of C5 complement, resulting in defective opsonization. These patients respond to antibiotics and infusions of fresh-frozen plasma or whole blood.

Seborrheic Dermatitis in Adults

The clinical picture and course of this disease differ in adults and infants.

Seborrheic eczematid is the mildest form of the disease (eczematid = eczema-like, dermatitis-like). It is associated with seborrhea, scaling, mild redness, and often pruritus of the scalp, eyebrows, nasolabial folds, and retroauricular area, as well as over the sternum and the shoulder blades (see Figs. 126-1 to 126-4). Asymptomatic, fluffy white dandruff of the scalp represents the mild end of the spectrum of seborrheic dermatitis and has been referred to as *pityriasis sicca*.

Erythema paranasale, more common in young women than men, may be part of this disease spectrum.

Patchy seborrheic dermatitis is the classic, well-known disease with chronic recurrent lesions. Lesions have a predilection for scalp, temples, retroauricular folds and external ear canals (Fig. 126-3), inner parts of the eyebrows and glabella with nasolabial folds (Fig. 126-2), and V-shaped areas of the chest and back (*eczema mediothoracicum*). Less frequently, intertriginous areas such as the side of the neck, axillae, submammary region, umbilicus, and genitocrural folds are involved. Skin lesions are characterized by a yellow color, mild to severe erythema, mild inflammatory infiltrate, and oily, thick scales and crusts. This has occasionally been referred to as *pityriasis steatoides*. Patients report pruritus, particularly on the scalp and in the ear canal. The lesions start with follicular and perifollicular redness and mounds; they spread until they form clearly outlined, round to circinate (petaloid) patches (Greek *petalon*, a thin plate or leaf). The pityriasiform type of seborrheic dermatitis is seen on the trunk and mimics the lesions of pityriasis rosea, producing oval scaly lesions whose long axes tend to parallel the ribs. In some individuals only one or two sites are involved. Chronic otitis externa may be the sole manifestation of seborrheic dermatitis. Another possible manifestation is blepharitis, with honey-colored crusts along the rim of the eyelid and casts of horny cell debris around the eyelashes. In men, a more follicular type of seborrheic

dermatitis may extend over large parts of the back, flanks, and abdomen.

Course

Usually the disease lasts for years to decades with periods of improvement in warmer seasons and periods of exacerbation in the colder months. Widespread lesions may occur as a result of improper topical treatment or sun exposure. The extreme variant of the disease is a generalized exfoliative erythroderma (seborrheic erythroderma).

Differential Diagnosis

The differential diagnosis varies from site to site: *scalp*: dandruff, psoriasis, atopic dermatitis, impetigo; *ear canal*: psoriasis or contact dermatitis, irritant or allergic; *face*: rosacea, contact dermatitis, psoriasis, impetigo; *chest and back*: pityriasis versicolor, pityriasis rosea; *eyelids*: atopic dermatitis, psoriasis, *Demodex folliculorum* infestation (demodicosis, demodicidosis); *intertriginous areas*: psoriasis, candidiasis.

Therapy

In general, therapy is directed toward loosening and removal of scales and crusts, inhibition of yeast colonization, control of secondary infection, and reduction of erythema and itching. Patients should be informed about the chronic nature of the disease and understand that therapy works by controlling the disease rather than by curing it.

Infants

Scalp

Treatment consists of the following measures: removal of crusts with 3 to 5% salicylic acid in olive oil or a water-soluble base; warm olive oil compresses; application of low-potency glucocorticoids (e.g., 1% hydrocortisone) in a cream or lotion for a few days; mild baby shampoos; proper skin care with emollients, creams, and soft pastes.

Intertriginous Areas

Treatment measures include drying lotions, such as 0.2 to 0.5% dioquinol in zinc lotion or zinc oil. In cases of candidiasis, nystatin or amphotericin B lotion or cream can be applied followed by soft and stiff pastes. In cases of oozing dermatitis, application of 0.1 to 0.25% gentian violet (solutio pyoctanini) in combination with cotton or muslin diapers is often helpful. Imidazole preparations (e.g., 2% ketoconazole in soft pastes, creams, or

lotions) may also be effective.

Adults

Because the disease runs an unpredictably long course, careful and mild treatment regimens are recommended. Anti-inflammatory agents and, when indicated, antimicrobial or antifungal agents have to be used.

Scalp

Daily shampoo with shampoos containing 1 to 2.5% selenium sulfide, antifungals (e.g., ketoconazole), zinc pyrithione, benzoyl peroxide, salicylic acid, coal or juniper tar, or detergents is recommended. Crusts or scales can be removed by overnight application of glucocorticoids or salicylic acid in water-soluble bases or, when necessary, under occlusive dressings. Tinctures, alcoholic solutions, hair tonics, and similar products usually aggravate the inflammatory state and should be avoided.

Face and Trunk

Patients should avoid greasy ointments and reduce or omit the use of soaps. Alcoholic solutions or pre- or aftershave lotions should not be recommended. Low-potency glucocorticoids (1% hydrocortisone is usually sufficient) are helpful early in the course of the disease; uncontrolled long-term applications will lead to side effects such as steroid dermatitis, steroid rebound phenomenon, steroid rosacea, and perioral dermatitis.

Antifungals

Good results are achieved with topical application of antifungal agents, especially imidazoles. Usually 2% preparations in the form of shampoos and creams are used. Double-blind studies report 75 to 95 percent improvement. In these trials, however, only ketoconazole[42,43,44,45,46] or itraconazole[42] were studied; other imidazoles such as econazole, clotrimazole, miconazole, oxiconazole, isoconazole, and ciclopiroxolamine may also be effective. Allylamine antifungals such as terbenafine solution (1%) may also be effective.[47] Comparative studies are lacking. The authors' personal experience, though based on open, uncontrolled studies only, is best with ketoconazole cream. Imidazoles, like other antifungal agents, have a wide spectrum of effects, including anti-inflammatory properties and inhibition of cell wall lipid synthesis.[15] Their efficacy is not proof of a causal relationship between *P. ovale* and seborrheic dermatitis.

Metronidazole

Topical metronidazole is a worthwhile alternative in the treatment repertoire of seborrheic dermatitis. It has made its successful debut in patients with rosacea. Extemporaneous formulations (up to 2% in a cream base) or commercial products (0.75% gel, MetroGel) are used once or twice daily. There are no formal studies, and the drug is registered for the treatment of rosacea only. This recommendation is based on the authors' experience.

Seborrheic Otitis Externa

Seborrheic otitis externa can be best treated with a low-potency glucocorticoid cream. Many otic preparations (solutions) contain neomycin, which is a strong sensitizer, and should therefore be avoided. Once dermatitis is under control, the glucocorticoid should be discontinued and a solution containing aluminum acetate be applied once or twice daily to maintain control. This acts as a drying agent and reduces the microbial flora.

Seborrheic Blepharitis

Special consideration is given to the treatment of seborrheic blepharitis. The use of hot compresses with gentle debridement with a cotton-tipped applicator and baby shampoo one or more times daily is recommended. Stubborn cases may require the use of a topical antibiotic such as sodium sulfacetamide ophthalmic ointment. The possible use of ocular preparations containing glucocorticoids should be referred to an ophthalmologist.

Pityriasis Amiantacea

The scales should be removed by the use of cade oil (juniper tar) ointment or a topical tar/salicylic ointment. Either preparation should be washed out of the scalp after 4 to 6 h with a suitable shampoo, e.g., tar or imidazole shampoo. Potent topical glucocorticoid scalp creams or liquids may be beneficial in some cases, preferably under plastic occlusion in the initial phase. A vitamin D analogue (calcipotriol cream or lotion, or tacalcitol ointment) is also recommended and useful in selected patients. If topical treatment fails, systemic glucocorticoids (e.g., 0.5 mg prednisolone per kg body weight daily for about 1 week) in combination with topical treatment (steroid under occlusion, followed by open application) is worthwhile. Concomitant antimicrobial treatment (e.g., macrolides, sulfonamides) is reserved for stubborn cases, especially if bacterial coinfection of the scalp is

treatment of tinea pedis can help to prevent the development of a life-threatening cellulitis. Intertrigo needs to be prevented as it can be a portal of entry for irritants and infectious agents. Prevention of venous ulcers and of allergic contact dermatitis needs to be meticulous in patients with gravitational eczema who are dangerously prone to both of these complications. Elderly skin is more prone to traumatic lacerations. Aged skin which is edematous is particularly susceptible to trauma and bulla formation.

Skin Atrophy

Skin atrophy can be compounded due to a poor understanding of the correct use of medications, leading to misuse of topical steroids in the elderly patient, who may have associated edema with vascular insufficiency. The geriatric dermal-epidermal interface is already compromised. The fragile skin of the poorly groomed foot is a setup for fissures, bullae, infection, and further loss of the ability to be mobile.

Seborrheic Dermatitis

(See Chap. 126)

Although seborrheic dermatitis can affect all ages and both males and females, it becomes much more common with increasing age. The association with increasing age correlates best in men, whereas women have a peak in morbidity after puberty, after which it gradually declines. There appears to be a cephalocaudad progression of the location with increasing age. Although the face and head are the predominant sites in younger age groups and certainly can be severely affected in the elderly, genitocrural and lower extremity lesions increase with age. The pubis, crural folds, gluteal cleft, and penis (seborrheic balanitis) may be involved. Lesions may be misdiagnosed as tinea infections. Striking flares of seborrheic dermatitis have been associated with confining illnesses such as coronary infarction. Exacerbations may eventuate in a diffuse erythroderma, which is often misdiagnosed. Pathogenesis may be related to changes in the cutaneous microflora. A neurophysiologic role is suggested by the association of seborrheic dermatitis with mental retardation and with Parkinson's disease. Seborrheic dermatitis may appear abruptly in the elderly, heralding the onset of Parkinson's disease. The scalp is usually involved, often giving rise to a mistaken diagnosis of dandruff. Simple dandruff declines late in adult life.

Intertrigo

Intertrigo is more frequent in the elderly due to redundant skin folds and environmental factors, including temperature, moisture, friction, and inadequate hygiene. Polymicrobial secondary colonization and subsequent infection can occur. No one organism can be singled out as the main agent.

Treatment of the Cutaneous Signs of Aging

Multiple medical and surgical therapeutic modalities are evolving for the treatment of the outward signs of intrinsic aging and photoaging. See Table 146-3.

Some publications still use the obsolete term *premature skin aging* to describe alterations in unprotected skin, notably the face and sun-exposed areas, implying that this is merely exaggerated manifestations of normal aging. However, the evidence is convincing that photoaging is not simply an acceleration of the inevitable age-dependent alterations. Photoaging denotes the gross and microscopic cutaneous changes that are a consequence of chronic solar radiation. Recent studies demonstrate that this spectrum of changes is often diametrically opposed to that which occurs in intrinsically aged skin.[4,64,65] Sun worshippers do look prematurely aged, and this is the basis for the common misconception. Those who scrupulously avoid the sun can reach the ninth decade with smooth, unblemished skin that shows only mild thinning, loss of elasticity, and a deepening of normal expression lines. By contrast, at age 50, serious sun worshippers, especially those of skin phototype I (blue-eyed, fair-skinned, Celtic ancestry who burn easily and tan poorly), have a plethora of wrinkles, with yellowed, lax, dry, leathery, knobby, blotchy skin and a variety of benign, premalignant, and malignant neoplasms.

Late nineteenth century dermatologists, notably Unna and Dubreuilh, clearly recognized the baleful influence of sunlight by comparing the integument of farmers and sailors to that of indoor workers. This was at a time when the leisured class stayed out of the sun. Today, a tan is prized by Caucasians and is ironically equated with health and beauty. Because decades of extensive sun bathing can occur before the photoaging changes become apparent to the naked eye,[12] there is a lack of urgency concerning prevention. This latent period also reinforces the impressions that actinically damaged skin differs only quantitatively from intrinsic aging. However, photoaging has distinctive and unique features that are quite different from normal aging.

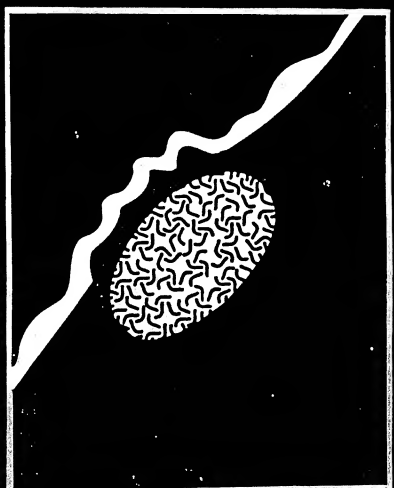
Appendix B

A Little, Brown Manual

Manual of Dermatologic Therapeutics

Fifth Edition

Kenneth A. Arndt



29 Seborrheic Dermatitis and Dandruff

I. **Definition and pathophysiology.** Seborrheic dermatitis and dandruff may each cause a scaling on the scalp that is often associated with itching. There are, however, distinctions that can be found between the two disorders. Dandruff is noninflammatory, increased scaling on the scalp that represents the more active end of the spectrum of physiologic desquamation. On a normal scalp, approximately 487,000 cells/sq cm can be found after a detergent scrub; scalps affected with dandruff and seborrheic dermatitis liberate up to 800,000 cells/sq cm.

Seborrheic dermatitis is an inflammatory, erythematous, and scaling eruption that occurs primarily in "seborrheic" areas, i.e., those with a high number and activity of sebaceous glands, such as the scalp, face, and trunk. Although seborrheic dermatitis occurs in neonatal and postpubertal life—times during which sebaceous glands are most active—no direct relationship between the amount or composition of sebum and the presence of dermatitis has been documented. Patients produce no more sebum on their scalps than do controls, and reducing sebum excretion affects neither dandruff nor seborrheic dermatitis. This disease is one of accelerated epidermal growth resulting in retention of nuclei in stratum corneum cells that have not had sufficient time to completely mature. On a normal scalp there are approximately 3700 nucleated cells/sq cm; on scalps with dandruff there are 25,000, and on those with seborrheic dermatitis the count is 76,000. Follicular occlusion may be a primary event, with yeast overgrowth in the folliculitis associated with seborrheic dermatitis.

It has been postulated that prolonged retention of sebum on the skin may in some way act as an irritant or alter epidermal function following its percutaneous reentry. *Pityrosporum ovale*, a lipophilic yeast which is a normal inhabitant of the skin, has been hypothesized to be the etiologic agent in seborrheic dermatitis. There is a significantly increased incidence—and often particular severity—of seborrheiclike dermatitis in patients with AIDS (Grossier, 1989; Marino, 1991). More direct support comes from reports that seborrheic dermatitis responds to oral and topical ketoconazole, an imidazole effective against *Pityrosporum* (see sec. IV.F). No evidence of immediate or delayed hypersensitivity reactions to *P. ovale* has been demonstrated in seborrheic dermatitis. Higher than normal total serum IgG or IgA level has been found in some patients. Often noted and equally intriguing is the increased incidence of seborrheic dermatitis in Parkinson's disease (idiopathic and drug-induced) and other neurologic disorders; one study demonstrated improvement in 10 patients with the use of isotretinoin, implicating an increase in the residual sebum pool due to immobility. *P. ovale* has been cultured in 73% of infants with seborrheic dermatitis; the yeast may be cultured from the scalp, face, and presternal or inguinal region.

II. **Subjective data.** The lesions of seborrheic dermatitis and dandruff are often asymptomatic, but pruritus is not uncommon and may be intense at times.

III. **Objective data**

A. Dandruff appears simply as noninflammatory, diffuse scaling on the scalp only.

B. With seborrheic dermatitis, there is erythema, scaling, and at times exudation; the borders may be well defined. Mild erythema and fine, dry scaling also may be found on the eyebrows, eyelids, nasolabial and postauricular folds, moustache, beard, and presternal areas. Inframammary folds, groin, gluteal crease, and umbilicus are also affected. Lesions may become thick, semiconfluent, yellow, and greasy. Secondary impetiginization and folliculitis may occur. Seborrheic dermatitis may be a cause of a generalized exfoliative erythroderma.

C. Seborrheic marginal blepharitis, which consists of erythema and scaling of eyelid margins and cilia, is often associated with mild granular conjunctivitis. Seborrheic dermatitis in other sites is often not present.

D. Infantile seborrheic dermatitis is characterized by erythema and scaling plaques involving the scalp, diaper region, or flexural surfaces; when the vertex of the scalp is involved, the condition is know as cradle cap. Generalized exfoliative dermatitis in an infant secondary to seborrheic dermatitis is referred to as Leiner's syndrome with or without a defect in the fifth component of complement.

E. Drug eruptions from gold therapy may mimic seborrheic dermatitis, as may a vitamin B–deficient diet.

IV. **Therapy**

A. Agents effective in eliminating the scaling of daodruff and seborrheic dermatitis appear to act by varying mechanisms. Selenium sulfide (see Chap. 40, Cleansing Agents, sec. I.F.2) and tars (see Chap. 40, Keratolytic, Cytotoxic, and Destructive Agents, sec. XVII) inhibit mitotic activity, and selenium kills yeasts as well. Zinc pyrithione (see Chap. 40, Cleansing Agents, sec. I.F.3) is directly cytotoxic and has antimicrobial effects, and salicylic acid (see Chap. 40, Keratolytic, Cytotoxic, and Destructive Agents, sec. XIV) disrupts the bonds that cause stretum corneum cells to stick together. There are no studies comparing the efficacies of antiseborrheic shampoos. The following egents are listed in rough eppreximation of usefulness:

1. **Ketoconazole** (Nisoral) shampoo is used at least twice weekly.
2. Shampoos containing 2½% **selenium sulfide** (Selsun) should be applied 2–3 times weekly for 5–10 minutes each time.
3. Preparations containing 1–2% zinc pyrithione (Danex, DHS-Zinc, Head and Shoulders, Zincon) work almost as well.
4. **Salicylic acid–sulfur shampoos** (Ionil, Sebulex) are less effective but show definite activity.
5. Tar shampoos (DHS-T, Ionil T, Pentrax, Sebutone, T/Gel, Zetar) inhibit epidermal proliferation through cytostatic effects after an initial burst of transient hyperplasia.
6. **Chloroxine** (Capitrol) shampoo contains a synthetic antibacterial compound similar to the hydroxyquinoline compounds used in dermatology for many years. Comparative efficacy studies with this shampoo are unavailable.
7. Any nonmedicinal shampoo, particularly those containing **surfactants** and **detergants**, will remove scales and lead to subjective clinical improvement and decreased desquamation for about 4 days. These agents should be used every 2 days to control dandruff.

B. If the lesions are extensive or very inflammatory, also have the patient apply either a topical corticosteroid solution, lotion, or spray. (Valisone or Diprosone lotion is generally effective; Synalar or Lidex solution and other corticosteroid lotions are also useful.) Alternatively, a 10% sodium sulfacetamide lotion bid–tid may be used.

C. Ketoconazole (Nizoral), an imidazole with action against *P. ovale*, has been reported effective for seborrheic dermatitis when given either orally (200 mg PO daily), topically (2% cream applied bid), or as a 2% shampoo. Topical ketoconazole has been studied in children and shown to be effective and well tolerated. Its efficacy is approximately equivalent to that of 1% hydrocortisone cream. Oral ketoconazole has too many potential adverse reactions to warrant its use in this condition.

D. Thick crusts may be removed more easily by overnight applications of a keratolytic gel, with or without plastic cap occlusion; 3% sulfur, 3% salicylic acid, 4% cetyl alcohol–coal tar distillate (Pragmatar) cream; Baker's P&S liquid; 20-10-5 ointment (see Chap. 27, sec. V.B.6) or a 30-minute compress with warm mineral oil prior to shampooing.

E. Seborrheic dermatitis lesions on other areas respond rapidly to a corticosteroid cream such as 1% hydrocortisone applied 1–3 times a day. Aerosols or lotions are easier to apply to hairy areas. Prolonged application of high-potency fluorinated corticosteroids may lead to disfiguring telangiectasis and atrophy. Other useful topical agents for glabrous skin include sulfur-containing medications such as 10% sulfacetamide lotion; 3% sulfur, 3% salicylic acid, 4% cetyl alcohol–coal tar distillate (Pragmatar) cream; or formulations such as precipitated sulfur 3–10%, salicylic acid 1–5%, and tar 2% in an ointment base or 1–3% sulfur in calamine lotion.

F. Seborrheic blepharitis is treated 1–3 times a day with either sulfacetamide alone or a 10% sulfacetamide, 0.2% prednisolone, 0.12% phenylephrine suspension (Blephamide, Vasocidin) or similar preparations (Cetapred, Metimyd, Optimyd). It is essential to monitor intraocular tension concurrent with intermittent or chronic steroid therapy in or around the eye.

G. Topical lithium succinate ointment used daily for 8 weeks showed remission or marked improvement compared with placebo in 30 patients with seborrheic dermatitis; it is presumed to act as an anti-inflammatory agent.

H. A 15% propylene glycol solution applied to the scalp reduced the number of *P. ovale* and improved seborrheic dermatitis in 90% of those treated.

I. Ultraviolet light (both UVA and UVB) are inhibitory to the growth of *P. ovale*. Many individuals note improvement of seborrheic dermatitis during the summer months.

References

Berghrant, I. M., et al. An immunological study in patients with seborrheic dermatitis. *Clin. Exp. Dermatol.* 16:331–338, 1991.

Binder, R. L., and Jonelis, F. J. Seborrheic dermatitis in neuroleptic-induced parkinsonism. *Arch. Dermatol.* 119:473–475, 1983.

Burton, J. L., and Pye, R. J. Seborrhea is not a feature of seborrheic dermatitis. *Br. Med. J.* 286:1168–1170, 1983.

Cowley, N. C., Farr, P. M., and Shuster, S. The permissive effect of sebum in seborrheic dermatitis: An explanation of the rash in neurological disorders. *Br. J. Dermatol.* 122:71–76, 1990.

Cuelenaere C., de Berseques, J., and Kint, A. Use of topical lithium succinate in the treatment of seborrheic dermatitis. *Dermatology* 18:194–197, 1992.

Faergemann, J. Treatment of seborrheic dermatitis of the scalp with ketoconazole shampoo: A double-blind study. *Acta Derm. Venereol. (Stockh.)* 70:171–172, 1990.

Faergemann, J. Propylene glycol in the treatment of seborrheic dermatitis of the scalp: A double-blind study. *Cutis* 42:69–71, 1988.

Groisser, D., Bottone, E. J., and Lebwohl, M. Association of *Pityrosporum orbiculare (Malassezia furfur)* with seborrheic dermatitis in patients with acquired immunodeficiency syndrome (AIDS). *J. Am. Acad. Dermatol.* 20:770–773, 1989.

Hill, M. K., et al. Skin surface electron microscopy in *Pityrosporum* folliculitis: The role of follicular occlusion in disease and the response to oral ketoconazole. *Arch. Dermatol.* 126:181–184, 1990.

Kieffer, M., et al. Immune reactions to *Pityrosporum ovale* in adult patients with atopic and seborrheic dermatitis. *J. Am. Acad. Dermatol.* 22:739–742, 1990.

Marino, C. T., McDonald, E., and Romano, J. F. Seborrheic dermatitis in acquired immunodeficiency syndrome. *Cutis* 48:217–218, 1991.

Marks, R., Pearse, A. D., and Walker, A. P. The effects of a shampoo containing zinc pyrithione on the control of dandruff. *Br. J. Dermatol.* 112:416–422, 1985.

McGrath, J., and Murphy, G. M. The control of seborrheic dermatitis and dandruff by antipityrosporal drugs. *Drugs* 41:178–184, 1991.

Priestly, G. C., and Brown, J. C. Acute toxicity of zinc pyrithione to human skin cells in vitro. *Acta Derm. Venereol. (Stockh.)* 60:145–148, 1980.

Ruiz-Maldonado, R., et al. *Pityrosporum ovale* in infantile seborrheic dermatitis. *Pediatr. Dermatol.* 6:16–20, 1989.

Shuster, S. The aetiology of dandruff and the mode of action of therapeutic agents. *Br. J. Dermatol.* 111:235–242, 1984.

Skinner, R. B., et al. Double-blind treatment of seborrheic dermatitis with 2% ketoconazole cream. *J. Am. Acad. Dermatol.* 12:852–856, 1985.

Wikler, J. R., et al. The effect of UV-light on *Pityrosporum* yeasts: Ultrastructural changes and inhibition of growth. *Acta Derm. Venereol. (Stockh.)* 70:69–71, 1990.

Appendix C

Handbook of Nonprescription *Drugs*

Published by
American Pharmaceutical Association
The National Professional Society of Pharmacists
2215 Constitution Avenue, NW
Washington, DC 20037

should be avoided in intertriginous areas because of their maceration potential. Also, in an acute process, ointments may cause further irritation because of their occlusive effect.

- Aerosols, gels, or lotions may be recommended when the dermatitis affects a hair-covered area of the body.

A large number of cosmetic dry skin formulations are commercially available. These may contain natural oils, vitamins, or a variety of fragrances that have a psychologic appeal. However, the fragrances and dyes found in many of these formulations may be irritating or allergenic to sensitive dry skin and should be avoided.

Efficacy of any skin care product may need to be sacrificed or compromised somewhat to achieve patient acceptance. The most efficacious product that the patient will accept should be recommended.

Topical nonprescription products come in various package sizes and strengths. Table 3 lists the amount of drug needed to cover a given area of the body three times daily over a 3-week period. By being aware of such details, the pharmacist can serve the patient economically as well as therapeutically.

Scaly Dermatoses

Dandruff, seborrheic dermatitis (seborrhea), and psoriasis are described as chronic, scaly dermatoses. They may be placed on a spectrum ranging from dandruff, a minor problem that is primarily cosmetic, to psoriasis, a clinical condition that can have significant physical, psychologic, and economic consequences. (See Table 4 for the distinguishing features of these three dermatoses.)

Part of the body	Cream/ointment (g)	Lotion/solution/gel (mL)
Face	5–10	100–120
Both hands	25–50	200–240
Scalp	50–100	200–240
Both arms or both legs	100–200	240–360
Trunk	200	360–480
Groin and genitalia	15–25	120–180

Adapted from Bingham EA. Topical dermatologic therapy. In: Rook A, Parish LC, Beare JM, eds. *Practical Management of the Dermatologic Patient.* Philadelphia: JB Lippincott; 1986: 227–8.

Nonprescription products are appropriate for all degrees of dandruff. Many cases of seborrheic dermatitis will respond to the same nonprescription drug regimen used to treat dandruff. Psoriasis that involves mild inflammation may be responsive to nonprescription treatment. However, initial diagnosis and management of acute flare-ups require the attention of a physician.[29]

Specific Conditions

Dandruff

Dandruff is a chronic, noninflammatory scalp condition that results in excessive scaling of scalp epidermis. Dandruff is clinically visible in approximately 20% of the population. Severity declines in the summer and is not proved to be aggravated by emotional states. Authorities disagree over whether inadequate shampooing exacerbates dandruff; however, there is agreement that a consistent washing routine is important in managing the condition.[29,30]

Etiology and Characteristics Dandruff is not a true disease; rather, it is a physiologic event and condition much like the growth of hair and nails, except that the end product is visible on the scalp and has a substantial cosmetic and social stigma associated with its presence. It correlates with the proliferative activity of the epidermis. Dandruff generally appears at puberty, reaches a peak in early adulthood, levels off in middle age, and declines in advancing years (occurring only rarely after age 75).

Dandruff is characterized by accelerated epidermal cell turnover, an irregular keratin breakup pattern, and the shedding of cells in large scales. It is normal for epidermal cells on the scalp to continually slough off just as they do on other parts of the body. It is also normal for the epidermal cell turnover rate to be greater on the scalp than on other parts of the body. In dandruff patients, however, the epidermal cell turnover rate on the scalp is about twice that of normal scalp.[7] This rate also assists in distinguishing dandruff from seborrhea and psoriasis; psoriasis has a higher rate than seborrhea, which has a higher rate than dandruff.

Dandruff is diffuse rather than patchy; it is not inflammatory; and pruritus is common. Scaling, the only visible manifestation of dandruff, is the result of an increased rate of horny substance production on the scalp and the sloughing of large scales. Dandruff scales often appear around a hair shaft because of the epithelial growth at the base of the hair. This phenomenon does not occur on the normal scalp because the horny substance breaks up in a much more uniform fashion. The horny layer of the scalp normally consists of 25–35 fully keratinized, closely coherent cells per square millimeter arranged in an orderly fashion. However, in dandruff, the intact horny layer has fewer than 10 normal cells per square millimeter, and nonkeratinized cells are common. With dandruff, crevices occur deep in the stratum corneum, resulting in cracking, which generates relatively large scales. If the large scales are broken down to smaller units, the dandruff becomes less visible.

As the rate of keratin cell turnover increases, so too

Table 1 Differentiating features of dandruff, seborrhea, and psoriasis

	Dandruff	Seborrhea	Psoriasis
Location	Scalp	Adults and children: head and trunk Children only: back, intertriginous areas	Scalp, elbows, knees, trunk, and lower extremities
Exacerbating factors	Generally a stable condition, exacerbated by inadequate washing, dry climate	Exacerbated by many external factors, notably stress and low relative humidity	Exacerbated by mechanical irritation, stress, climate, drugs, infection, endocrine factors
Appearance	Thin, white, or grayish flakes; even distribution on scalp	Patchy lesions with margins; mild inflammation; oily, yellowish scales	Usually symmetrical, red, patchy plaques with sharp border; silvery-white scale; small bleeding points when removed. Difficult to distinguish from seborrhea in early stages or in intertriginous zones
Inflammation	Absent	Present	Present
Epidermal hyperplasia	Absent	Present	Present
Epidermal kinetics	Turnover rate is two times faster than normal	Turnover rate is about five to six times faster than normal	Turnover rate is about five to six times faster than normal
Percentage of incompletely keratinized cells	Rarely exceeds 5% of total corneocyte count.	Commonly makes up 15–25% of corneocyte count	Commonly makes up 40–60% of corneocyte count

Information extracted from:
Wright DE. In: Clark C, ed. *Self-Medication: A Reference for Health Professionals*. 3rd ed. Ottawa: Canadian Pharmaceutical Association; 1988: 87.
McGinley KJ et al. *J Invest Dermatol*. 1969; 53: 107.
Kligman AM et al. *J Soc Cosmet Chem*. 1974; 25: 73.

does the number of incompletely keratinized cells, a situation characterized by the retention of nuclei in keratin layer cells. Incompletely keratinized cells in dandruff appear in clusters, possibly as a result of tiny inflammatory foci that are incited when capillaries discharge a load of inflammatory cells into the epidermis, causing accelerated epidermal growth in a small area. These microfoci are found on all scalps but are increased proportionately in dandruff.[7]

The specific cause of accelerated cell growth seen in dandruff is unknown. There is continuing debate over whether dandruff is a result of elevated microorganism levels—particularly of the yeast *Pityrosporum ovale*.[30]

Treatment Dandruff is more of a cosmetic than a medical problem, and treatment is fairly straightforward. The patient needs to understand that there is no direct cure for dandruff and that the condition can usually be well controlled. Washing the hair and scalp with a nonmedicated shampoo every other day or even daily is often sufficient to control dandruff. If it is not, medicated nonprescription antidandruff products may be recommended. With medicated shampoos, contact time improves effectiveness. The patient should be counseled to allow medicated shampoo to remain on the hair for approximately 1 minute before rinsing and repeating. Thorough rinsing is important in the use of all shampoo products.

A cytostatic agent such as pyrithione zinc, selenium sulfide, or coal tar is recommended. These agents reduce the epidermal turnover rate. However, the coal tar–containing shampoos may tend to discolor light hair as well as clothing and jewelry and thus may not appeal to some patients. Next, a keratolytic shampoo containing salicylic acid or sulfur may be used. If dandruff proves resistant to these agents, the patient should be referred to a physician for treatment.[29,31]

Seborrheic Dermatitis

Seborrheic dermatitis is a general term for a group of eruptions that occur predominantly in the areas of greatest sebaceous gland activity (eg, the scalp, face, and trunk). This condition affects approximately 12 million Americans. Seborrhea occurs mostly in middle-aged and elderly persons, particularly men. It is often found in persons with parkinsonism, endocrine states associated with obesity, zinc deficiency, and human immunodeficiency virus infection. Quadriplegics and persons who have experienced a cerebrovascular accident (stroke) or a myocardial infarct (heart attack) also seem prone to seborrhea. Because nonprescription therapy is effective in a significant percentage of cases, the pharmacist can play a key role in the management of seborrhea.[32]

Etiology and Characteristics Seborrhea is marked by accelerated epidermal proliferation and sebaceous gland activity.[19] The distinctive characteristics of the disorder are its common occurrence in hairy areas (especially the scalp); the appearance of dull, yellowish-red lesions, which are well demarcated; and the associated presence of oily-appearing, yellowish scales. Pruritus is common.[33] The most common form, seborrhea of the scalp, is characterized by greasy scales on the scalp that often extend to the middle third of the face with subsequent eye involvement. (See color plates, photograph 10.) Lesions may also appear in the external auditory canal and around the ear. When seborrhea of the scalp occurs in newborns and infants, it is referred to as cradle cap and is treated primarily by gentle massaging with baby oil followed by a nonmedicated shampoo to remove the scales. Pruritus does not appear to accompany cradle cap, and the condition often clears spontaneously by 8–12 months of age.[31,29,32]

The cause of seborrhea is unknown although predisposition appears to be a genetic trait. Emotional and physical stress serve as aggravating factors. Proposed etiologic factors have included vitamin B complex deficiency, food allergies, autoimmunity, climate changes, and low relative humidity. The characteristic accelerated cell turnover and enhanced sebaceous gland activity give rise to the prominent scale displayed in the condition; however, there is no clear-cut quantitative relationship between the degree of sebaceous gland activity and susceptibility to seborrhea.

It is almost universally accepted that seborrhea is merely an extension of dandruff, and the controversy regarding the involvement of *P ovale* extends to seborrhea. Some researchers, however, dispute the link with dandruff, offering evidence that seborrhea is a separate condition. Incompletely keratinized cells commonly make up 15–25% of the corneocyte count in seborrheic dermatitis but rarely exceed 5% in dandruff.[7,32]

Assessment The differential assessment of seborrheic dermatitis is usually straightforward. However, whereas dandruff is considered a relatively stable condition, seborrhea fluctuates in severity, often as a result of stress. Involvement of eyebrows and eyelashes, with concurrent blepharitis, is associated with seborrhea but not with dandruff. Moreover, dandruff is considered a noninflammatory condition whereas seborrhea is usually accompanied by erythema and sometimes crusting.

Lesion distribution is a key factor in distinguishing seborrhea from psoriasis. Seborrhea commonly involves the face and generally is not found on the extremities, whereas psoriasis is rarely found on the face but is commonly found on bony prominence such as the elbows and knees. However, the scalp is generally involved in both conditions, and if this is the only site of involvement, differential assessment is difficult. Physical appearance of scales may help to differentiate the two disorders. Seborrhea is usually marked by oily, yellow scales whereas psoriatic scales are generally dry and silvery in appearance. Additionally, the presence of the Auspitz sign (small bleeding points) is indicative of psoriasis.

Fungal infections may be mistaken for seborrhea. Thus, proper assessment is important because fungal infections may be worsened by seborrhea therapy using hydrocortisone. If the lesion is located in the groin, tinea cruris (jock itch) must be considered, especially during warm weather. Scalp lesions must be evaluated for the possibility of tinea capitis (ringworm of the scalp).[7]

Treatment The treatment of seborrheic dermatitis is similar to that of dandruff. Seborrhea generally responds to shampoos containing pyrithione zinc, selenium sulfide, salicylic acid, or coal tar. However, frequent use of selenium sulfide may make the scalp oily and may actually exacerbate the seborrheic condition.

A primary difference between the treatment of dandruff and that of seborrhea is the use of topical corticosteroids. These products are not indicated for dandruff but may be used in the management of seborrheic dermatitis whenever erythema is persistent after therapy with medicated shampoos. Hydrocortisone lotions for scalp dermatitis are available without a prescription. The patient should be instructed to apply the hydrocortisone product two to three times a day until symptoms subside and then intermittently to control acute exacerbations. The patient should also be instructed in the proper technique of application. The hair should be parted and the product applied directly to the scalp and massaged in thoroughly. This process should be repeated until desired coverage of the affected area is achieved. The absorption of medication into the scalp is enhanced if the lotion is applied after shampooing; skin hydration promotes drug absorption.

The patient should be encouraged to minimize prolonged and continued use of hydrocortisone in the treatment of seborrheic dermatitis because a rebound flare may occur when prolonged therapy is discontinued. If the condition worsens or if symptoms persist for more than 7 days, a physician should be consulted. At this point, a more potent topical steroid may be indicated.[7]

If the seborrhea spreads to the ear canal, eyelashes, or eyelids, a physician should be consulted for appropriate therapy. This may include the use of prescription otic and ophthalmic agents.

Nonprescription products used to treat seborrhea are to be avoided for children under 2 years of age, except under the advice and supervision of a physician.[34]

Psoriasis

Psoriasis is estimated to afflict 1–3% of the US population. Lesions are often localized but may become gener-

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Manfred Bohn et al.

Serial No. 10/606,229

Filing Date: June 26, 2003

USE OF 1-HYDROXY-2-PYRIDONES FOR THE TREATMENT OF SEBORRHEIC DERMATITIS

DECLARATION OF KEVIN KRIEL

I, Kevin Kriel, do hereby declare that:

1. I have been employed by Medicis Pharmaceutical Corporation ("Medicis") since November 2002, and was a consultant to Medicis from January 2002 to November 2002. I am currently Senior Product Manager, and am responsible for the sales and marketing of Loprox® Shampoo. I am also a registered pharmacist and hold a degree in pharmacy from Albany College of Pharmacy. According to legal counsel, Loprox® Shampoo is a ciclopirox-containing shampoo covered by claims 14, 15, 17, 18, 19, 20, 22, and 23 of this patent application.
2. My job responsibilities with respect to Loprox® Shampoo requires me to be familiar with seborrheic dermatitis, available treatments for seborrheic dermatitis, as well as the issues, preferences, and concerns that physicians and patients have concerning seborrheic dermatitis and treatments for it.
3. No other ciclopirox shampoo is currently marketed in the U.S. to date.
4. There are other seborrheic dermatitis treatments on the market in the U.S. They use a variety of active ingredients and delivery vehicles.

5. Seborrheic dermatitis frequently affects highly visible areas of the skin, such as the head (scalp and face) or the hands. Patients regard it as a socially embarrassing, sometimes even a disfiguring disorder. For this reason, physicians and patients place the highest priority on effectiveness, of any treatment for seborrheic dermatitis. Price is often no consideration, or only a distant secondary consideration, in treating seborrheic dermatitis.

6. Loprox® Shampoo is promoted on the basis of its effectiveness, never on the basis of price. In fact, physicians and patients regard Loprox® Shampoo as so effective that Loprox® Shampoo is successfully sold at a premium price. This is further proof that the treatment is effective and only available with Loprox® Shampoo.

7. Loprox® Shampoo is taking market share from its closest competitors as seen in the sales data provided here. Most, if not all of these competitors are less expensive than Loprox® Shampoo. Therefore, it is clear that treatment of seborrheic dermatitis with a 1-hydroxy-2-pyridone (e.g. ciclopirox) composition with no additional actives, a pH between about 4.5 to about 6.5, and a surfactant is really desired by patients and physicians.

8. Loprox® Shampoo is a very successful product. Since January 2005, the market has essentially remained flat (with a 1% decrease in total prescriptions). Loprox® Shampoo's total number of prescriptions grew about 13% from January 2005 to June 2006[1] (when the sales are analyzed at six month intervals).

9. This 13% growth in sales of Loprox® Shampoo occurred at the expense of competitive prescription products. While Loprox® Shampoo sales have grown, the

[1] This is the most current month's data available at this time.

total number of prescriptions in the market has been constant, or slightly declined. (The total number of prescriptions written for products in this market declined 1% from January 2005 to June 2006, when the sales are analyzed at six month intervals). Therefore, the growth in Loprox® Shampoo sales represents a turning away from other treatments and reflects a growing preference for Loprox® Shampoo among physicians and their patients. As I mentioned in Paragraph 5, effectiveness is a paramount concern to physicians and patients. This growth in Loprox® Shampoo sales reflects a judgment by physicians and patients that Loprox® Shampoo is a more effective treatment for seborrheic dermatitis.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application and any registration resulting therefrom.

Date: 9/20/2006

Kevin Kriel

X. Related Proceedings Appendix

Appellants attach the Board's prior Decision in Appeal No. 2004-0309 (in parent application no. 09/077,194), mailed September 15, 2004. Also, Appellants filed a Notice of Appeal in application no. 09/077,194 on July 24, 2007, and intend to file an Appeal Brief in due time.

CPE- JLS

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

03804. 1596

Paper No. 48

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte MANFRED BOHN, KARL THEODOR KRAEMER, and ASTRID MARKUS

Appeal No. 2004-0309
Application No. 09/077,194

DECISION ON REQUEST FOR REHEARING

Before WINTERS, MILLS, and GREEN, Administrative Patent Judges.

WINTERS, Administrative Patent Judge.

ON REQUEST FOR REHEARING

Pursuant to the provisions of 37 CFR § 41.52, applicants request rehearing of our decision mailed September 15, 2004 (Paper No. 46), vacating the examiner's final rejections of claims 38 through 42, 48, and 53 through 66; and entering new grounds of rejection under 37 CFR § 41.50(b).

On rehearing, applicants' main argument is that we have misinterpreted the claim language "a method of treating a human or animal patient in need of treatment for seborrheic dermatitis." According to applicants, (1) we have interpreted the language

DL 12-27-04

too broadly; (2) the claim language does not "read on" treating mere symptoms of seborrheic dermatitis (Request for Rehearing, paragraph bridging pages 2 and 3); and (3) the appealed claims should be construed to require an intent to treat a human or animal patient suffering from seborrheic dermatitis, or to require administering applicants' compositions to patients suffering from seborrheic dermatitis with the intent to cure the underlying condition (id., page 4). We disagree.

Jansen Distinguished

In espousing their position, applicants rely principally on Jansen v. Rexall Sundown, Inc., 342 F.3d 1329, 68 USPQ2d 1154 (Fed. Cir. 2003). That reliance is misplaced.

In Jansen, appeal was taken from the final decision of the United States District Court for the Southern District of Indiana granting summary judgment that Rexall Sundown, Inc. has not infringed Jansen's U.S. Patent Number 4,945,083. In affirming that decision, the Federal Circuit applied "the mode of claim interpretation . . . used by courts in litigation, when interpreting the claims of issued patents in connection with determinations of infringement or validity." In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1321 (Fed. Cir. 1989). This is not, however, "the mode of claim interpretation . . . applicable during prosecution of a pending application before the PTO." Id. at 321, 13 USPQ2d at 1322.

As stated in In re Zletz, 893 F.2d at 321-22, 13 USPQ2d 1322:

> During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow. When the applicant states the meaning that the claim terms are intended to have, the claims are examined with that meaning, in order to achieve a complete exploration of the applicant's invention and its relation to the prior art. See In re Prater, 415 F.2d 1393, 1404-05, 56 CCPA 1381, 162 USPQ 541, 550-51 (1969) (before the application is granted, there is no reason to read into the claim the limitations of the specification). The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breath of language explored, and clarification imposed. Burlington Industries, Inc. v. Quigg, 822 F.2d 1581, 1583, 3 USPQ2d 1436, 1438 (Fed.Cir.1987; In re Yamamoto, 740 F.2d 1569, 1571, 222 USPQ 934, 936 (Fed.Cir.1984). The issued claims are the measure of the protected right. United Carbon Co. v. Binney & Smith Co., 317 U.S. 228, 232, 63 S.Ct. 165, 167, 87 L.Ed. 232, 55 USPQ 381, 383-84 (1942)(citing General Electric Co. v. Wabash Appliance Corp., 304 U.S. 364, 369, 58 S.Ct. 899, 901-02, 82 L.Ed. 1402, 37 USPQ 466, 468-69 (1938). An essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.

Applicants' position to the contrary, notwithstanding, Jansen does not set forth a rule of claim interpretation applicable during prosecution of pending applications before the PTO. During patent examination, applicants' claims "must be interpreted as broadly as their term reasonably allow" and "there is no reason to read into the claim[s] the limitations of the specification."

As stated in Jansen, 342 F.3d at 1333, 68 USPQ2d at 1158, the court's conclusion respecting the meaning of claim language "is bolstered by an analysis of the prosecution history." The court stated that:

> In this case, the "treating or preventing macrocytic-megaloblastic anemia" phrase and the "to a human in need thereof" phrase were added to gain

> allowance of the claims after almost twenty years of repeatedly unsuccessful attempts to gain allowance of claims without those phrases. We must therefore give them weight, for the patentability of the claims hinged upon their presence in the claim language. See Smith v. Magic City Kennel Club, Inc., 282 U.S. 784, 790, 51 S.Ct. 291, 75 L.Ed. 707 (1931) ("The applicant[,] having limited his claim by amendment and accepted a patent, brings himself within the rules that if the claim to a combination be restricted to specified elements, all must be regarded as material, and that limitations imposed by the inventor, especially such as were introduced into an application after it had been persistently rejected, must be strictly construed against the inventor and looked upon as disclaimers."). Furthermore, because both phrases were added simultaneously to overcome the same rejection, they should be read together, meaning that the word "thereof" in the phrase "to a human in need thereof" should be construed to refer to the treatment or prevention of macrocytic-megaloblastic anemia. Finally, that "need" must be recognized and appreciated, for otherwise the added phrases do not carry the meaning that the circumstances of their addition suggests that they carry. In other words, administering the claimed vitamins in the claimed doses for some purpose other than treating or preventing macrocytic-megaloblastic anemia is not practicing the claim method, because Jansen limited his claims to treatment or prevention of that particular condition and those who need such treatment or prevention. Thus, the '083 patent claims are properly interpreted to mean that the combination of folic acid and vitamin B_{12} must be administered to a human with a recognized need to treat or prevent macrocytic-megaloblastic anemia.

Id. at 1333-34, 68 USPQ2d at 1158 (emphasis added). But no such facts have been established here. Applicants do not point to prosecution history in this case, similar to that outlined in Jansen, which would give rise to a narrow claim construction based on estoppel or disclaimer.

Furthermore, the claims in Jansen are restricted to methods of treating or preventing macrocytic-megaloblastic anemia in humans; and "the issue reduces to whether such a human must know that he is in need of either treatment or prevention of that condition." Jansen, 342 F.3d at 1333, 68 USPQ2d at 1157. The claims before us,

however, are drawn to "a method of treating a human or animal patient in need of treatment for seborrheic dermatitis" (emphasis added).

In conclusion, Jansen is distinguishable from the present case because (1) Jansen was decided on appeal from a District Court decision granting summary judgment in a patent infringement suit, where a different mode of claim interpretation applied; (2) applicants do not point to prosecution history here, similar to that outlined in Jansen, which would give rise to a narrow claim construction; and (3) the method claims in Jansen are restricted to human subjects compared with the broader claims before us, drawn to "a method of treating a human or animal patient in need of treatment for seborrheic dermatitis."

Intent to Treat vs. Intent to Cure

Applicants argue that their claimed invention is not anticipated by, or obvious from, the cited prior art because the prior art does not disclose that compositions recited in the appealed claims are administered to patients suffering from seborrheic dermatitis with the intent to cure the underlying condition (Request for Rehearing, paragraph bridging pages 4 and 5). That argument, however, is predicated on faulty claim construction which relies on a limitation not present in applicants' claims.

Based on our review of the specification, the only passage which refers to a "cure" of seborrheic dermatitis appears at page 2, lines 1 through 4:

> In comparison to ketoconazole, the substances according to the invention - even after only a short topical contact time - concentrate rapidly in the skin layers which are relevant for fungal growth and thus contribute to a rapid cure. (Emphasis added).

It is improper, however, to import limitations from the specification into claims in a pending application. See, In re Zletz, 893 F.2d at 1321, 13 USPQ2d 1322 (Before the application is granted, there is no reason to read into the claim the limitations of the specification). The claims are the measure of the protected right, and an essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous. (Id.). Here, applicants' claims are couched in terms of treating ("a method of treating a . . . patient in need of treatment for seborrheic dermatitis"). Manifestly, treating is not the same a curing, and we shall not construe applicants' claims as requiring an "intent to cure the underlying condition."

Applicants' argument that the appealed claims should be construed to require an intent to treat a human or animal patient suffering for seborrheic dermatitis (Request for Rehearing, page 4, first full paragraph) or an intent to cure the underlying condition (Id., paragraph bridging pages 4 and 5) underscores the need "to fashion claims that are precise, clear, correct, and unambiguous." In re Zletz, 893 F.2d at 1322, 13 USPQ2d at 1322.

"Consisting Essentially Of"

Applicants argue that claims 38, 40 through 42, 48, and 65 patentably distinguish over Saint-Leger in view of the transition phrase "consisting essentially of" (Request for

Rehearing, Section II., pages 5-9). According to applicants, the recitation of an active component in those claims "consisting essentially of" at least one 1-hydroxy-2-pyridone of formula (I) excludes the halogenated antibacterial agent disclosed by Saint-Leger. We disagree.

As stated in PPG Indus., Inc. v. Guardian Indus. Corp., 156 F.3d 1351, 1355, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998),

> By using the term "consisting essentially of," the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention. A "consisting essentially of" claim occupies a middle ground between closed claims that are written in a "consisting of" format and fully open claims that are drafted in a "comprising" format. (Emphasis added).

Here, applicants' argument that "consisting essentially of" excludes the halogenated antibacterial agent of Saint-Leger is an example of ipse dixit reasoning. Applicants do not describe the "basic and novel properties of the invention," or explain why or establish how the halogenated antibacterial agent of Saint-Leger materially affects those properties.

Additionally, it is apparent from applicants' specification (page 7, line 36 through page 8, line 16) that the composition of the claimed method may include a host of ingredients or additives. On this record, it is unclear why the halogenated antibacterial agent of Saint-Leger would "materially affect" the basic and novel properties of the invention and, accordingly, be excluded by the phrase "consisting essentially of;" whereas the host of ingredients listed in the specification do not materially affect the

basic and novel properties of the invention and, accordingly, are included by the phrase "consisting essentially of." Applicants have not made it clear, in their specification or in their Request for Reconsideration, what they "regarded as constituting a material change in the basic and novel characteristics of the invention." Id., 156 F.3d at 1355, 48 USPQ2d at 1355.

Matters Not Addressed in the Request for Rehearing

The appealed claims are not limited to a method of treating a human or animal patient in need of treatment for patchy seborrheic dermatitis, the classic, well-known disease with chronic recurrent legions (Exhibit A, page 8). In their Request for Rehearing, applicants do not deny that the term "seborrheic dermatitis" includes a disease spectrum; or that "[a] symptomatic, fluffy white dandruff of the scalp represents the mild end of the spectrum of seborrheic dermatitis and has been referred to as pityriasis sicca" (Exhibit A, page 8). Further, applicants do not deny that "[m]any cases of seborrheic dermatitis will respond to the same nonprescription drug regimen used to treat dandruff" (Exhibit C, page 550, column 2, lines 2 through 4).

Conclusion

In conclusion, for the reasons set forth, we adhere to our original decision vacating the examiner's final rejections of claims 38 through 42, 48, and 53 through 66; and entering new grounds of rejection under the provisions of 37 CFR § 41.50(b).

Having carefully reviewed applicants' Request for Rehearing, we decline to modify our original decision or opinion in any respect. Accordingly, the Request is denied.

DENIED

Sherman D. Winters
Administrative Patent Judge

Demetra J. Mills
Administrative Patent Judge

Lora Green
Administrative Patent Judge

BOARD OF PATENT APPEALS AND INTERFERENCES

Finnegan, Henderson, Farabow,
Garrett & Dunner
Franklin Square Bldg., Suite 700
1300 I Street, NW
Washington, DC 20005-3315

dem